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Early Syphilis Among Men Who Have Sex with Men in the US Pacific Northwest, 2008–2013: Clinical Management and Implications for Prevention

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Abstract

Substantial increases in syphilis during 2008–2013 were reported in the US Pacific Northwest state of Oregon, especially among men who have sex with men (MSM). The authors aimed to characterize the ongoing epidemic and identify possible gaps in clinical management of early syphilis (primary, secondary, and latent syphilis ≤1 year) among MSM in Multnomah County, Oregon to inform public health efforts. Administrative databases were used to examine trends in case characteristics during 2008–2013. Medical records were abstracted for cases occurring in 2013 to assess diagnosis, treatment, and screening practices. Early syphilis among MSM increased from 21 cases in 2008 to 229 in 2013. The majority of cases occurred in HIV-infected patients (range: 55.6%–69.2%) diagnosed with secondary syphilis (range: 36.2%–52.4%). In 2013, 119 (51.9%) cases were diagnosed in public sector medical settings and 110 (48.0%) in private sector settings. Over 80% of HIV-infected patients with syphilis were in HIV care. Although treatment was adequate and timely among all providers, management differed by provider type. Among HIV-infected patients, a larger proportion diagnosed by public HIV providers than private providers were tested for syphilis at least once in the previous 12 months (89.6% vs. 40.0%; $p < 0.001$). The characteristics of MSM diagnosed with early syphilis in Multnomah County remained largely unchanged during 2008–2013. Syphilis control measures were well established, but early

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syphilis among MSM continued to increase. The results suggest a need to improve syphilis screening among private clinics, but few gaps in clinical management were identified.

Introduction

Syphilis infections have increased in recent years internationally,[1] as well as throughout the United States, especially among men who have sex with men (MSM).[2–4] After sustained decreases to an all-time low in 2000, rates of primary and secondary syphilis in men in the United States increased from 3.0 cases per 100,000 population in 2001 to 9.8 in 2013.[2,3] In 2013, MSM accounted for 75% of primary and secondary syphilis cases in 49 states and the District of Columbia that provided information about sex of sex partners.[2] The surge in syphilis among MSM is troubling, considering the morbidity associated with untreated syphilis, including neurosyphilis and cardiovascular sequelea.[5] Furthermore, syphilis is associated with both HIV transmission and acquisition,[6–9] and a disproportionate number of syphilis diagnoses occur in HIV-infected MSM.[10,11]

Control of syphilis requires early detection and treatment to prevent further transmission. During the early stages when patients are most infectious, patients and clinicians may not recognize signs and symptoms (i.e., painless chancre, atypical rash) as syphilis;[12] thus, a key control measure is routine screening, including routine screening of MSM for syphilis.[13,14] Current guidelines recommend at least annual screening of all sexually active MSM for sexually transmitted diseases (STD).[15] For MSM at higher risk of acquiring STDs, more frequent screening may be indicated.[15,16]

Between 2008 and 2013, the state of Oregon in the Pacific Northwest United States experienced a greater than 8-fold increase in the incidence of early syphilis, from 1.2 to 10.1 cases per 100,000 population;[2,17] 58% of cases occurred among residents of Multnomah County, and 95% of these cases were among MSM. Multnomah County is the most populous county in Oregon and includes the city of Portland.

Despite coordinated public health measures to increase awareness among the populations at risk and dissemination of information about the epidemic through letters to providers, public announcements, and citywide infectious disease grand rounds, rates of early syphilis in Multnomah County continued to increase. In this investigation, we examined demographic and clinical characteristics of early syphilis among MSM residents of Multnomah County during 2008 through 2013, and evaluated clinical management of MSM diagnosed in 2013 by stage of infection and HIV status. Our aims were to characterize the ongoing epidemic and to identify possible gaps in clinical management to guide future public health interventions.

Methods

Oregon regulations mandate health-care providers to report suspected syphilis cases, and laboratories to report positive treponemal and nontreponemal syphilis tests to the local health department.[18] Syphilis tests include nontreponemal serologic tests [rapid plasma reagin (RPR) and veneral disease research laboratory (VDRL) tests] and treponemal tests

[fluorescent treponemal antibody absorption (FTA-ABS) test, treponema pallidum particle agglutination assay (TPPA) test, and enzyme immunoassay (EIA)]. Confirmed and suspected syphilis cases, identified using either traditional or reverse sequence syphilis testing algorithms, are investigated through a structured interview to elicit demographic, behavioral, and clinical information, ensure appropriate treatment, and identify sex partners who may have been exposed. Data are recorded on a standardized form and entered into the Multnomah County Health Department (MCHD) electronic database.

Study Population

We used the MCHD reportable disease database to identify male residents of Multnomah County with clinical or laboratory confirmed diagnosis of early syphilis (primary, secondary, or latent syphilis ≤1 year) during January 1, 2008 through December 31, 2013 and who self-reported oral/anal sex with a man in the 12 months before their syphilis diagnosis.

Data Collection

For cases diagnosed during 2008 through 2013, we used the MCHD database to extract demographic and clinical data, including age, race/ethnicity, stage of infection, and HIV status. HIV status is self-reported or laboratory-confirmed in the MCHD database. For cases diagnosed in 2013, we abstracted medical records for incident syphilis infections from public and private clinics that reported the cases. An incident syphilis infection was defined as the first time a case patient had a reactive RPR test and evidence of a confirmed or presumptive infection in the medical record in 2013.

Data collected include stage of infection, history of syphilis, previous syphilis tests, signs and symptoms on exam, evidence of more than one provider visit before diagnosis (as determined by documented self-report or multiple provider visits for the same signs and symptoms), RPR titer at diagnosis, diagnosing and treating providers, treatment received, duration from syphilis test to initial treatment, and laboratory-confirmed HIV status. We collected both diagnosing and treating providers to assess patients who received treatment from a different clinic than where they were diagnosed.

For HIV-uninfected patients, HIV testing at the time of the syphilis test and use of pre-exposure prophylaxis (PrEP) were collected. For HIV-infected patients, antiretroviral (ARV) use, HIV RNA, and CD4 count were collected from the state reportable disease database. To assess routine testing practices, we compared syphilis testing in the previous 12 months among HIV-infected MSM diagnosed with syphilis by the MCHD public HIV clinic to other clinic settings. The MCHD public STD clinic was not included in this analysis as this clinic performs only episodic, not routine, care.

We classified providers by type of clinic as follows: MCHD public STD clinic as “STD Providers,” MCHD public HIV clinic as “HIV Providers,” and other clinic types including one large academic center, three large medical systems/managed care organizations, two private practice primary care clinics, and one public primary care clinic as “ Other Providers.” Stage of infection was categorized as primary, secondary, and early latent syphilis using Centers for Disease Control and Prevention (CDC) surveillance case definitions for syphilis.[2]

Statistical Analyses

For cases diagnosed during 2008 through 2013, trends in case characteristics by year of diagnosis were examined in 2-year increments due to small sample sizes in 2008 and 2009. To examine categorical variables, we used the Cochran-Mantel-Haenszel test with nonparametric modified ridit scores; this test is similar to the non-parametric Wilcoxon test and enhances the analysis when the parameter is not normally distributed.[19,20] For continuous variables, the Spearman's rank correlation was used.

For cases diagnosed in 2013, only the incident diagnosis for individuals with more than one syphilis diagnosis during 2013 was used for analysis; because only incident syphilis infections were used, we refer to these cases as patients. Descriptive analyses were used to assess clinical management, including diagnosis, treatment, and screening. Differences by provider type and HIV status were examined using χ^2 test or Fisher's exact test for proportions and Wilcoxon test for medians. One patient with newly diagnosed HIV at the time of the syphilis test was excluded because he would not have had an opportunity to be in HIV care, unlike cases with a known history of HIV. All statistical analyses were conducted using SAS version 9.3 (SAS Institute, Inc., Cary, NC).

This evaluation was determined to be public health practice and not constitute human subjects research according to the criteria from the Office of Research Protection by the Oregon Health Authority and according to the Human Subject Review's decision code by CDC's Epidemiology Program Office; therefore, the evaluation did not require IRB review.

Results

Demographic and clinical characteristics of MSM diagnosed with early syphilis during 2008–2013

From 2008 to 2013, a total of 663 cases of early syphilis were diagnosed in MSM in Multnomah County; the number of cases increased each year from 21 in 2008 to 229 in 2013 (Fig. 1). Case distribution by stage of infection did not change significantly over time (p_{trend} = 0.713). Across all years, most cases occurred in non-Hispanic whites (72.3% in 2008–2009, 75.7% in 2010–2011, and 72.0% in 2012–2013). Median age increased significantly from 36 years (interquartile range (IQR): 30–44) in 2008–2009 to 39 years (IQR: 31–48) in 2012–2013 (p_{trend} = 0.009). Most patients were HIV-infected, and the proportion of cases among HIV-infected patients increased from 55.6% during 2008–2009 to 69.2% during 2012–2013 (p_{trend} = 0.016).

Clinical characteristics and management of MSM diagnosed with early syphilis in 2013

In 2013, a total of 229 cases of early syphilis were diagnosed among MSM, 119 (51.9%) in public sector medical settings and 110 (48.0%) in private sector settings. Medical records were available for all 64 cases diagnosed by STD providers, all 52 cases diagnosed by HIV providers, and 87 (77%) cases diagnosed by other providers. Ten patients were diagnosed with syphilis twice in 2013. Among the remaining 193 incident cases, 24.9% were primary, 42.5% were secondary, and 32.6% were early latent syphilis (Table 1).

Median time to treatment differed by stage of infection; most patients with primary syphilis received treatment on the same day they were tested for syphilis (median 0 day, IQR: 0–2 days), whereas most patients with secondary syphilis received treatment a median of 2 days (IQR: 0–4 days), and with early latent syphilis a median of 3 days (IQR: 1–6 days) after their syphilis test ($p < 0.001$). Three (6.3%) patients with primary syphilis and 19 (23.3%) patients with secondary syphilis had more than one provider visit for the same symptoms before diagnosis, and several misdiagnoses were noted in the medical chart. Misdiagnoses for patients subsequently diagnosed with primary syphilis included chancroid and herpes simplex virus and for secondary syphilis included contact dermatitis, eczema, allergy, pityriasis rosea, scarlet fever, and scabies.

Clinical management differed by provider type (Table 1). All patients received treatment for syphilis; 83.3% were treated with one dose of benzathine penicillin, 11.0% with three doses of benzathine penicillin, and 5.8% with doxy-cycline. Most patients diagnosed by STD providers received treatment on the same day they were tested for syphilis (median 0 day, IQR: 0–3 days), whereas most patients diagnosed by HIV providers received treatment the next day (median 1 day, IQR: 0–5 days), and those diagnosed by other providers a median of 3 days (IQR: 1–6 days) after their syphilis test ($p < 0.001$). Receipt of treatment in a clinic different from the diagnosing clinic occurred in 15.9% of patients diagnosed by other providers, 3.3% diagnosed by STD providers, and 2.1% diagnosed by HIV providers ($p = 0.006$); of these, all patients diagnosed by other providers and HIV providers received treatment from STD providers.

Patient characteristics and clinical management also differed by HIV status. A total of 128 (66.3%) patients were HIV-infected at the time of their syphilis test (Table 2). HIV-infected patients were older than HIV-uninfected patients (median age 41 vs. 33 years; $p = 0.001$), but did not differ by race/ethnicity. HIV-infected patients were more likely to have a history of past syphilis infection compared with HIV-uninfected patients (39.8% vs. 10.8%; $p < 0.001$). Most HIV-infected patients were diagnosed with early latent syphilis, while most HIV-uninfected patients were diagnosed with secondary syphilis ($p = 0.004$). There were three cases of neurosyphilis, all among HIV-infected patients; two in patients with secondary syphilis and one in a patient with early latent syphilis. There were no cases of ocular syphilis.

Median RPR titer at diagnosis was higher among HIV-infected patients compared with HIV-uninfected patients (1:64 vs. 1:32; $p < 0.001$). Most (80.0%) HIV-uninfected patients underwent HIV testing at the time of their syphilis test, 2 (3.1%) were documented to be on PrEP, and 38.3% had been tested for syphilis at least once in the previous 12 months. The majority (84.4%) of HIV-infected patients were documented to be on ARV and 99.2% had HIV RNA or CD4 count within the previous 6 months.

We further investigated syphilis testing among HIV-infected patients in the previous 12 months. More HIV-infected patients diagnosed with syphilis by HIV providers than other providers were tested for syphilis at least once in the previous 12 months (89.6% vs. 40.0%; $p < 0.001$), and a larger proportion were tested more frequently (≥2 tests, 3 to 6 months apart) by HIV providers than other providers (75.0% vs. 29.2%; $p < 0.001$).

Discussion

Our findings indicate that while the number of reported early syphilis cases among MSM residents of Multnomah County increased during 2008 through 2013, their demographic and clinical characteristics remained largely unchanged. A recent study using nationally representative data found racial/ethnic disparities in HIV and STDs, with black and Hispanic adults in the United States having a higher burden of HIV and STDs than their white counterparts.[21]

In contrast to the increase in syphilis seen in predominantly young MSM of color in most metropolitan areas of the United States,[3] MSM with early syphilis in Multnomah County tended to be older (>30 years of age) and non-Hispanic white. These differences likely mirror characteristics of the overall MSM population of Multnomah County. Our finding that over half of MSM with early syphilis in Multnomah County were HIV infected is congruent with national data and may reflect the larger syndemic of STD and HIV among MSM across the United States[3] and in other high income coun-tries.[10,11] In many developed countries, a high percentage of syphilis cases in MSM occur in HIV-infected MSM,[10,11] and the re-infection risk in these men is high.[11]

Many of the MSM with early syphilis in Multnomah County, including almost half with HIV infection, were diagnosed at private clinics or large medical centers. Almost all HIV-infected MSM were in care and had undetectable viral load, indicating high health care utilization and good compliance with HIV medications. This should provide an ideal opportunity for early detection and treatment of syphilis. However, nearly a quarter of MSM with secondary syphilis had more than one provider visit for the same symptoms before diagnosis, suggesting missed opportunities for diagnosis, and several misdiagnoses were observed during medical records review. In most instances, this occurred in patients seen in private practice clinic settings whose providers may be less likely to conduct sexual histories or may be unfamiliar with signs and symptoms of syphilis.

This study did not specifically evaluate reasons for the increase in syphilis in Multnomah County; however, similar increases are occurring in MSM across the United States.[2] The increasing use of PrEP to prevent HIV infection among HIV-uninfected MSM has been implicated in the rise in non-HIV STDs.[22] In our study, only a small percentage of MSM with syphilis infection were on PrEP. Assessment of PrEP use and STD rates among MSM in Multnomah County should be considered if PrEP use becomes more widespread in this community.

Patients with untreated syphilis during the infectious early stages may transmit the disease and remain at risk for progression to serious complications including neurosyphilis. The majority of cases in Multnomah County were treated in a timely manner,[23] especially at the public STD clinic where most patients received treatment on the same day as their syphilis test. However, among patients diagnosed in private clinic settings, median time to treatment for secondary syphilis was three days. The delay in treatment may be due to the lag in test results from private clinics where syphilis rapid RPR tests are not performed, private providers waiting for confirmatory test results before administering treatment, or from the larger proportion of cases in private clinics referred to the public STD clinic for treatment.

Providers in non-STD clinic settings may not stock benzathine penicillin, relying instead on referrals for treatment at the public STD clinic. One strategy to facilitate prompt treatment could be delivery of penicillin to community clinics by public health staff.[24] Field interviews and partner management services could then be performed on the same day the patient receives treatment in these clinics.

Our findings also suggest missed opportunities for syphilis screening, especially considering the high access to care in this population. The majority of MSM were diagnosed while symptomatic, and the proportion of asymptomatic cases diagnosed with early latent syphilis did not increase over time as might be expected if more screening was being performed.[14] Sexually active MSM should be screened at least annually for HIV infection and syphilis,[15] with more frequent HIV and STD testing (every 3–6 months) for MSM at highest risk.[25]

In studies assessing provider adherence to national guidelines for STD screening among HIV-infected MSM in HIV clinics in the United States, the annual syphilis screening rates ranged from 54% to 76%.[26,27] More frequent syphilis screening occurs even less, with one study finding only 20% of HIV-infected MSM in the United States had documentation of repeat tests (≥2 tests, >3 months apart) within the previous 12 months.[27] Mathematical models suggest increasing the frequency of syphilis screening among the highest risk MSM would have a greater impact on reducing the transmission and prevalence of syphilis compared with increasing the proportion of MSM tested for syphilis at least once per year.[16,28]

In our investigation, we found that providers at the public HIV clinic appeared to be routinely screening for syphilis, as suggested by the large proportion of MSM having evidence of prior syphilis testing and the high percentage diagnosed with early latent syphilis. However, among HIV-infected MSM diagnosed by private providers, fewer than half were documented to have been tested for syphilis in the previous 12 months.

A recent study found that providers often fail to include HIV and STD counseling and testing during routine health care visits for at-risk persons,[29] citing individual and institutional barriers, including lack of training and discomfort with conducting a sexual history, lack of time to address sexual health risks, and lack of knowledge for screening reimbursements for HIV/STD.[30] To increase STD/HIV screening of MSM by private providers, structural interventions such as screening protocols, reminder systems, chart prompts in electronic medical records, or automatic testing for syphilis when other tests are ordered, may be useful.[31–33]

Our assessment is subject to some limitations. First, cases whose medical charts were available for review may have differed from those whose records were not reviewed. More of the charts reviewed were for HIV-infected MSM in care, whereas more of the charts not reviewed were from small public and private clinics that see more HIV-uninfected MSM. Second, we were unable to account for within-subject correlation in the analysis of years 2008 through 2013 because it was not possible to de-duplicate cases in the MCHD database.

However, for 2013, the year in which we could delineate individual patients, there were only 10 MSM with repeat syphilis infections. Finally, some patients may have sought STD

screening at a clinic outside of their usual service provider rather than from their primary care or HIV care provider due to concerns of confidentiality or cost of testing. We were able to account for patients who attended the public STD or HIV clinics as we included all laboratory data from these sites in our analysis.

In summary, syphilis control measures in Multnomah County were largely well established during this investigation, but the rates of early syphilis among MSM continued to increase. Our analysis identified some need to increase provider knowledge to prevent delays in diagnosis, and the need to improve syphilis screening in private clinic settings. Otherwise, we found few gaps in clinical management that could have contributed to the dramatic increase seen in this population. Other studies have similarly found, even in settings with substantial resources, syphilis among MSM remains a stubborn problem.[1]

In addition to better recognition of signs and symptoms during physical examinations and implementation of screening recommendations, especially among clinicians in private practice,[34] successful control of syphilis among MSM might require biomedical interventions that are sustained and tailored to the given population.

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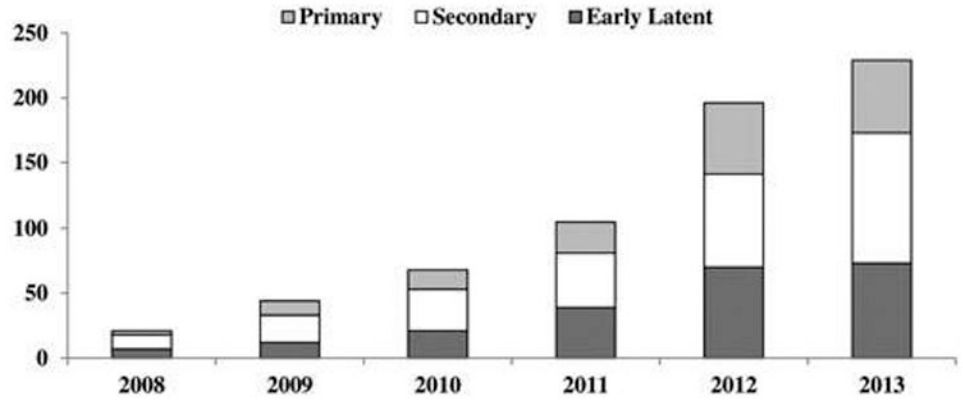

Fig. 1.

Early syphilis cases among men who have sex with men (MSM) by stage of infection, Multnomah County, 2008–2013 (n = 663). P_{trend} = 0.713; determined by Cochran-Mantel-Haenszel test with nonparametric modified ridit scores.

Table 1

Clinical Management of Men Who Have Sex With Men (MSM) with Early Syphilis by Diagnosing Provider, Multnomah County, 2013 (*n* = 193)

Characteristic	Total (*n* = 193)	STD providers (*n* = 62)	HIV providers (*n* = 48)	Other providers (*n* = 83)	*p*[a]
Stage of infection, *n* (%)					0.081
Primary	48 (24.9)	18 (29.0)	14 (29.2)	16 (19.3)	
Secondary	82 (42.5)	27 (43.6)	13 (27.1)	42 (50.6)	
Early latent	63 (32.6)	17 (27.4)	21 (43.8)	25 (30.1)	
Treatment, *n* (%)					**0.026**
Benzathine penicillin (1 dose)	159 (83.3)	55 (88.7)	45 (93.8)	59 (72.8)	
Benzathine penicillin (3 doses)	21 (11.0)	5 (8.1)	2 (4.2)	14 (17.3)	
Doxycycline	11 (5.8)	2 (3.2)	1 (2.1)	8 (9.9)	
Median time to initial treatment in days (IQR)[b]					
Overall	2 (0–5)	0 (0–3)	1 (0–5)	3 (1–6)	**<0.001**
Stage of infection					
Primary	0 (0–2)	0 (0–0)	0 (0–2)	0 (0–4)	
Secondary	2 (0–4)	0 (0–4)	0 (0–0)	3 (1–6)	
Early latent	3 (1–6)	0 (0–3)	4 (2–7)	4 (2–7)	
Treating provider differs from diagnosing provider, *n* (%)	16 (8.5)	2 (3.3)	1 (2.1)	13 (15.9)	**0.006**

[a]Determined by χ^2 test or Fisher's exact test for categorical variables and Wilcoxon test for medians;

[b]from syphilis test date. Numbers might not sum to column totals because of missing data.

IQR, interquartile range; STD, sexually transmitted disease.

Table 2

Characteristics of Men Who Have Sex With Men (MSM) with Early Syphilis by HIV Status, Multnomah County, 2013 (*n* =193)

Characteristic	HIV infected (*n* = 128)	HIV uninfected (*n* = 65)	*p*[a]
Median age in years (IQR)	41 (34–48)	33 (25–45)	**0.001**
Race/ethnicity, *n* (%)			0.291
White, non-Hispanic	95 (74.2)	44 (67.7)	
Black, non-Hispanic	6 (4.7)	4 (6.2)	
Hispanic	22 (17.2)	10 (15.4)	
Other	5 (3.9)	7 (10.8)	
History of syphilis, *n* (%)	51 (39.8)	7 (10.8)	**<0.001**
Stage of infection, *n* (%)			**0.004**
Primary	27 (21.1)	21 (32.3)	
Secondary	49 (38.3)	33 (50.8)	
Early latent	52 (40.6)	11 (16.9)	
Reason for exam, *n* (%)			**0.020**
Asymptomatic	24 (19.1)	2 (3.2)	
Symptomatic for STD-related symptoms	89 (70.6)	51 (81.0)	
Contact	13 (10.3)	10 (15.9)	
Diagnosing provider, *n* (%)			**<0.001**
STD providers	15 (11.7)	47 (72.3)	
HIV providers	48 (37.5)	0	
Other providers	65 (50.8)	18 (27.7)	
RPR, median titer (IQR)	1:64 (1:16–1:128)	1:32 (1:16–1:64)	**<0.001**
Treatment, *n* (%)			0.268
Benzathine penicillin (1 dose)	101 (78.9)	58 (89.2)	
Benzathine penicillin (3 doses)	16 (12.5)	5 (7.7)	
Doxycycline	9 (7.0)	2 (3.1)	
HIV testing, *n* (%)	–	52 (80.0)	–
PrEP use, *n* (%)	–	2 (3.1)	–
ARV use[b], *n* (%)	108 (84.4)	–	–
HIV RNA or CD4 count in previous 6 months, *n* (%)	127 (99.2)	–	–
HIV RNA ≤50 copies/mL, *n* (%)	82 (66.7)	–	–
Median CD4 cell count/mm^3 (IQR)	518 (378–726)	–	–

[a] Determined by χ^2 test or Fisher's exact test for categorical variables and Wilcoxon test for medians.

[b] Within 1 week before syphilis test date as documented in medical record. Numbers might not sum to column totals because of missing data.

ARV, antiretroviral; IQR, interquartile range; PrEP, pre-exposure prophylaxis; STD, sexually transmitted disease.